REMARKS

Overview

1. Claims 20, 25, 35, 44, 45, 47-49, 51 and 52 are objected to solely because they depend from a rejected claim.

2. Claims 1, 2, 5, 23, 39 and 53 are rejected as allegedly obvious over Akamatsu (USP 4,745,099) in view of newly relied on Anagnostou (USP 5,922,674).

3. Claims 26-30, 40-42, 46 and 50 are rejected as allegedly obvious over Akamatsu and Anagnostou, further in view of Delgado Hernandez (1999).

35 USC § 103(a) rejections

We do not agree with the Examiner that claims 1,2,5,23,39 and 53 are unpatentable over Akamatsu et al. in view of Anagnostou et al.

The Examiner states that Anagnostou et al. teach the use of human EPO to treat endothelial injury due to chemotherapy, radiation therapy, mechanical trauma, or to disease states which damage the endothelium (such as inflammation, heart disease or cancer). The Examiner further argues that "*it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of treating anemia of lung cancer by administering EPO as taught by Akamatsu et al. by formulating it to treat acute inflammation of the lungs with a reasonable expectation of success. The motivation and expected success is provided by the fact that the lungs are lined with endothelial cells and Anagnostou et al., who teach the use of human EPO to treat endothelial injury due to mechanical trauma, or to disease states which damage the endothelium, such as inflammation or cancer*".

We agree with the Examiner that Anagnostou et al. describe the use of EPO to treat endothelial injury. In the reference, it is described that EPO effectively can prevent and/or repair endothelial damage caused by e.g. inflammation. This is shown by *in vitro* experiments in a model of human umbilical vein

endothelial cells.

However, it is important to appreciate that the lungs are lined with epithelial cells and **not** endothelial cells. Epithelial cells (epithelium) and endothelial cells (endothelium) are different cell types which possess different functions.

Epithelial cells lines both the outside (skin) and the inside cavities and lumen of the body. Furthermore, epithelial cells line the insides of the lungs, the gastrointestinal tract, the reproductive and urinary tracts, and make up the exocrine and endocrine glands. Functions of epithelial cells include secretion, absorption, protection, transcellular transport, sensation detection, and selective permeability (cf. attached reference on Epithelium from Wikipedia). The epithelial cells of the lungs are derived from the endoderm. Alveolar epithelium consists of alveolar type 1 and 2 cells, both with high transport capacity for transepithelial solute and water transport, as well production of surfactant.

Endothelial cells line the interior surface of blood vessels, forming an interface between circulating blood in the lumen and the rest of the vessel wall. Endothelial cells are a specialized form of epithelial cells derived from the mesoderm. Endothelial cells are involved in many aspects of vascular biology, including vasoconstriction and vasodilation (i.e. regulation of blood pressure), blood clotting, formation of new blood vessels (angiogenesis) and control of passage of materials and cells into and out of the blood stream (cf. attached reference on Endothelium from Wikipedia). In general, endothelium cells in contrast to alveolar epithelial cells, do not have marked transepithelial transport capacities for solutes. Thus, the human umbilical vein endothelial cells employed in Anagnostou et al. are not representative of lung epithelial cells.

In conclusion, Anagnostou et al. does not motivate a man skilled in the art to modify the method described in Akamatsu et al. by formulating it to treat acute inflammation of the lungs, as the lungs are lined with epithelial cells and Anagnostou et

al. describe the use of EPO for prevention of damage of different type of cells, namely endothelial cells.

The same arguments apply for the rejection of claims 26-30, 40-42, 46 and 50 which are rejected under 35 U.S.C. 103(a) as being unpatentable over Akamatsu et al. and Anagnostou et al. in view of Delgado Hernandez et al.

Respectfully submitted,

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Enclosures
-Wikipedia "Epithelium" article
-Wikipedia "Endothelium" article

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